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Comparative Study of Placental Sonoelastography With Uterine and Umbilical Artery Doppler in a Tertiary Care Centre

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KEYWORDS

Sonoelastography, Uterine and Umbilical

ABSTRACT:

Background: Preeclampsia (PE) is a serious clinical condition that can lead to placental dysfunction, fetal growth retardation and fetal and maternal loss.

Objectives: The aim of this study is to reveal whether there is any relationship between placental shear wave elastography (SWE) values and umbilical artery and uterine artery doppler ultrasonography (US) findings, and to investigate the availability of SWE in early diagnosis of preeclampsia (PE).

Design: Cross sectional

Setting: Department of Radiodiagnosis at Shri Sathya Sai Medical College, Ammapettai, Chengalpattu- 603108, Tamil Nadu, India.

Patients And Methods: A cross-sectional study was conducted with 170 pregnant women within 20-32 weeks of gestation in radiology department. The study involved selecting patients for ultrasound examinations, obtaining written informed consent, and examining demographic characteristics, medical and obstetrical data. All ultrasound examinations were performed using a Mindray DC – 80 Exp system with a C 3-5 MHz curvilinear transabdominal and B-mode US and US elastography were performed in the supine position. Sonoelastography was performed using shear wave technique, and the placental image was centered in the field of view. A fixed-size ROI was placed at the center and edge of the placenta, and the quantitative placental stiffness value was displayed over a B-mode sonogram. Patients were asked to hold breaths during acquisition, and five samples were taken from each site.

Main Outcome Measures: Prediction of placental insufficiency and pre eclampsia using placental sonoelastography

Sample Size: 170 patients RESULTS: Of the 170 patients, the gestational age was 20-32 weeks, with a median of 23 weeks. Negative correlations were found between uterine and umbilical artery doppler parameters(PI and RI)with placental shear wave elasticity (SWE) and shear wave velocity (SWV) which were statistically significant . The study used ROC analysis to predict preeclampsia, with optimal results observed at a placental SWE cut-off value of ≥1.27 kPa and a SWV cut-off value of ≥1.15 m/s.

Conclusions: The study found significant correlations between Umbilical Artery pulsatility index (PI) and Uterine Artery PI, Umbilical Artery resistance index (RI), and Uterine Artery RI, with correlation coefficients of 0.343, 0.423, 0.374, and 0.454, respectively, all of which were statistically significant. The placenta elasticity with umbilical artery or uterine artery doppler findings showed inverse correlation.

INTRODUCTION

A placenta is an organ that nourishes and oxygenates the developing baby. When the placenta is healthy, the fetus is too. Intrauterine growth restriction (IUGR), oligohydramnios, pregnancy-induced hypertension, and fetal death can all be caused by abnormalities in the placenta. The placenta makes up one-sixth of the fetus's weight at term. The easiest way to gauge its size is to assess its placental thickness. With ultrasonography, the placenta's thickness can be easily measured. At the point where the cord is inserted, it is measured perpendicularly.[1] Gestational diabetes, hydrops fetalis, intrauterine fetal infections, and Rh-negative pregnancies are associated with thick placentas. Preeclampsia (PE) can result in fetal and maternal death, fetal growth retardation, and placental malfunction. When proteinuria and hypertension are present, PE can be diagnosed clinically. The tests that aid in its identification are biophysical profile, non-stress test (NST), Doppler ultrasonography (DUS), and ultrasonography (US). Findings from uterine artery and umbilical DUS may signal intrauterine growth retardation (IUGR) and PE early.[2,3] But none of the tests that have been developed thus far are sensitive enough

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to diagnose PE. The suppleness of placental tissue decreases as gestational age increases, and the placenta experiences increasing calcifications that cause it to stiffen. One method for determining the placenta's stiffness is called sono-elastography.[4] In Indian research, placental elasticity and uterine and umbilical artery Doppler indices are little understood. This is the only study on the Indian population that we are aware of that shows such a correlation. A complementary technique to traditional ultrasonography that gauges tissue elasticity is called sonoelastography. Shear wave elastography (SWE), also known as real-time sonoelastography, measures tissue hardness by measuring shear between target and reference tissue textures.[5,6] SWE is frequently utilized in liver, thyroid, prostate, and breast imaging to distinguish healthy tissue from neoplasia, inflammation, and fibrosis.[7,8] SWE in the placenta is used in a small number of scientific publications, nonetheless. This research aims to find out if there is a link between SWE levels and doppler results from the uterine and umbilical arteries, and to find out what the usual cut-off value is for predicting pregnancy-induced hypertension.

PATIENTS AND METHODS- Once a patient satisfied the inclusion criteria for this study, demographic characteristics, detailed medical and obstetrical data, and prenatal care charts were examined. All ultrasound examinations were performed with MINDRAY DC-80 6-MHz MF convex transducer. In all cases, B-mode US and US elastography were performed in the supine position. Sonoelastography was performed by using shear wave technique. The placental image was centered in the field of view. The fixed-size ROI, a rectangle measuring 1 × 0.5 cm, was placed at the center and edge of the placenta, and the quantitative placental stiffness value was displayed over a B-mode sonogram. The ROI was placed at homogeneous areas in the axial plane. The center and edge of the vessel-free placenta away from the cord insertion was selected as two sampling sites where fetal movements minimally affect the placenta. During acquisition, patients were asked to hold breaths at natural end-inspiratory phase. Five samples were taken from each site, from the center (sample 1) and edge (sample 2) of the placenta, and were averaged.[4]

RESULTS- Out of 170 patients studied, the study found statistically significant correlations between Umbilical Artery pulsatility index (PI) and Uterine Artery PI, Umbilical Artery resistance index (RI), and Uterine Artery RI, with correlation coefficients of 0.343, 0.423, 0.374, and 0.454, respectively, all of which were statistically significant (Figure 1). The study found strong negative correlations between the Umbilical artery PI and placental SWE; Umbilical artery RI and placental SWE and even stronger negative correlations between umbilical artery PI and placental SWV,which were statistically significant and indicating a potential health risk (Table 2). The study also found moderate negative correlations between the Uterine Artery pulsatility index (PI) and placental SWE;between Uterine Artery RI and placental SWE, with similar moderate negative correlations observed between Uterine Artery PI and placental SWV ; Uterine Artery RI and placental SWV (Table 3).The study used ROC analysis on placental SWE and SWV to predict risk of preeclampsia, with optimal results observed at a placental SWE cut-off value of ≥1.27 kPa and a SWV cut-off value of ≥1.15 m/s (Table 4).

Table 1: Details of the Placental sonography parameters

	N	Minimum	Maximum	Media (Q1-Q3)		
				Median	Q1	Q3
Gest age in weeks	170	20	32	26	23.0	30
UTERINE ARTERY PI	170	0.77	1.41	1.1	1.0	1.3
UTERINE ARTERY RI	170	0.38	0.77	0.6	0.5	0.7
UMBILICAL ARTERY PI	170	0.45	1.19	0.8	0.7	1.0
UMBILICAL ARTERY RI	170	0.45	0.64	0.5	0.5	0.6
PLACENTAL SHEAR WAVE VELOCITY	170	1.40	3.10	1.84	1.70	2.92
PLACENTAL SHEAR WAVE VELOCITY	170	0.80	1.58	1.14	0.90	1.41

Table 2: Correlation between Umbilical Artery PI and RI with Placental Shear Wave Elasticity and Velocity

		CENTALSWE	PLACENTAL SHEAR WAVE VELOCITY
UMBILICAL ARTERY PI	Pearson Correlation	-.767**	-.760**
	Sig. (2-tailed)	P<0.01	P<0.01
	N	170	170
UMBILICAL ARTERY RI	Pearson Correlation	-.822**	-.919**
	Sig. (2-tailed)	P<0.01	P<0.01
	N	170	170

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Table 3: Correlation between Uterine Artery PI and RI with Placental Shear Wave Elasticity and Velocity

		ACENTALSWE	PLACENTAL SHEAR WAVE VELOCITY
UTERINE ARTERY PI	Pearson Correlation	-.363**	-.406**
	Sig. (2-tailed)	P<0.01	P<0.01
	N	170	170
UTERINE ARTERY RI	Pearson Correlation	-.473**	-.463**
	Sig. (2-tailed)	P<0.01	P<0.01
	N	170	170

** Pearson`s correlation applied

Table 4: Area under curve and cut off value of Placental SWE andShear Wave Velocity for Predicting Pregnancy-Induced Hypertension

Test Result Variable(s)	AUC	P-Value	Asymptomatic95% ConfidenceInterval		Cut-offValue	Sensitivity	Specificity
			Lower Bound	Upper Bound			
Placental SWE	0.976	P<0.0001	0.960	0.993	1.27	92.8%	80.1%
Placental Shear Wave Velocity	0.89	P<0.0001	.979	.999	1.15	97.6%	91.8%

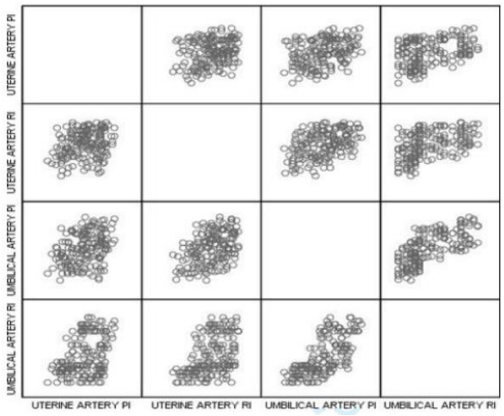

Figure 1: Correlation between Umbilical Artery PI and RI with Uterine artery PI and RI.

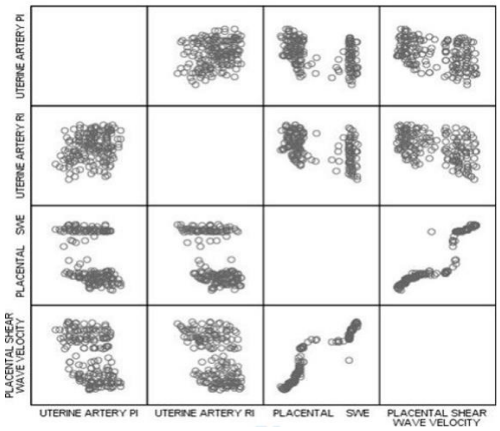

Figure 2: Correlation between Uterine Artery with Placental shear Wave Elasticity and Velocity

Figure 3: Elastography Image Demonstrating Anterior Placenta with Normal Elasticity (1.23kpa)

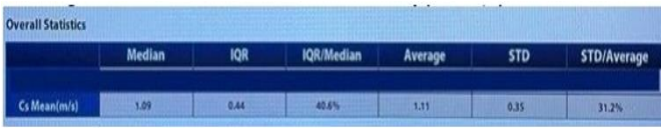

Figure 4: Normal Placental Shear Wave Velocity (1.09 m/s)

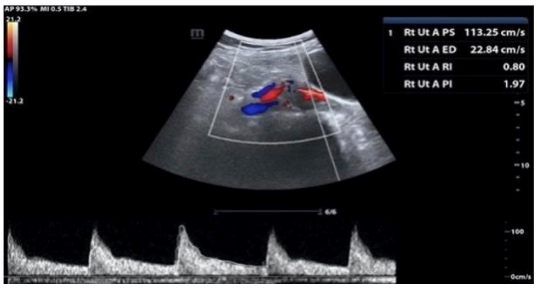

Figure 5: Normal Uterine Artery Doppler Indices At 28 Weeks

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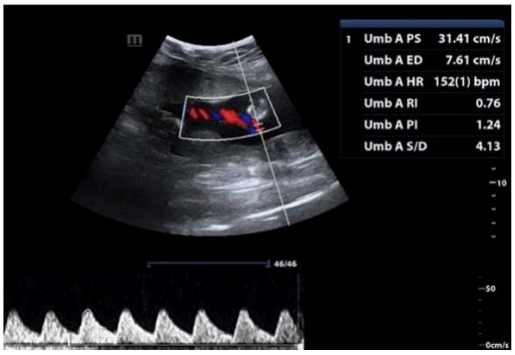

Figure 6: Normal Umbilical Artery Doppler Indices At 22 Weeks

Figure 7: Elastography Image Demonstrating Elevated Placental Elastography With IQR –2.34 kPa Predicting Pre-Eclampsia

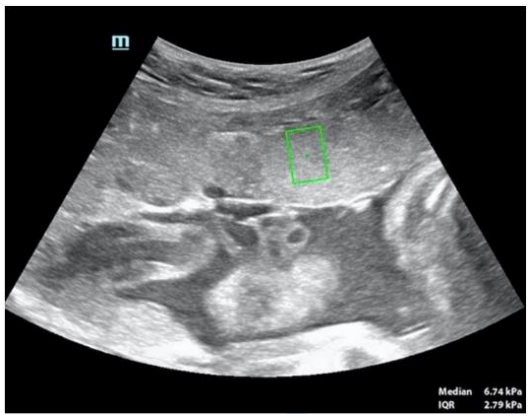

Figure 8: Elastography Image Demonstrating Elevated Placental Elastography At 28 Weeks with IQR – 2.79 kPa

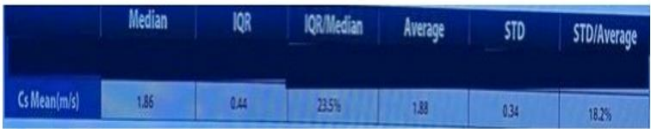

Figure 9: Elevated Placental Shear Wave Velocity (1.86 m/s)

DISCUSSION

This study was performed to correlate the placental elasticity with uterine and umbilical artery doppler indices. Previous studies showed that there was a correlation between placental elasticity and preeclampsia. It is unclear whether this difference is associated with placental insufficiency or placental insufficiency with IUGR. As a result of the increase in extracellular matrix proteins due to increased inflammation, elasticity in the placental tissue decreases.[10] This may lead to an increase in placental stiffness. For this reason, it can be considered that the elasticity of the placenta can be measured with US elastography to contribute to the diagnosis of PE. However, contrary to other tissues, studies on placental elasticity have not been performed for a long time due to the possibility that the increase in heat during use of US elastography may damage the fetus. Herman *et al.*[11] showed that during the study they performed, the increase in tissue heat during ultrasound elastography was within safe limits as determined by the FDA. Sugitani *et al.*[12] demonstrated that elastography does not thermally change histologically in the ex-vivo study performed on placenta and that US elastography is a safe assay. On these developments, in-vivo studies have been started with US elastography in the placenta. The majority of them were performed using the shear wave elastography method, two of which were animal experiments.[13-17] One of the two articles that studied placenta elasticity with strain elastography is an ex- vivo study,[9] by Durhan *et al.*, the other is an in-vivo study by Cimsit *et al.*[18] In the ex-vivo study, Sigutani *et al.* reported that the placenta was classified in three groups as IUGR, PE-diagnosed, and normal pregnancy. A statistically significant increase in placental stiffness was found in the group with IUGR compared to the normal group, but there was no statistically significant difference between PE patients and normal group. In both Cimsit *et al.*, and Kilic *et al.*[14] studies, patients with PE were collected in a single group regardless of the presence of IUGR, and they found a statistically significant increase in placental stiffness in this group according to the normal group of patients.[14,19] This may suggest that PE is not sufficient to cause an increase in placental stiffness and should be accompanied by IUGR. The first study showing placental elasticity as a strain was performed by Cimsit *et al.*[18] Doppler US abnormal findings are considered to be a weak positive predictors of placental insufficiency (8-33%).[19-21] Cimsit *et al.* found a correlation with elastography data by accepting notching

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in the uterine artery as a positive predictive factor for preeclpamsia. Kilic *et al.* found a weak correlation between the RI and PI values of the uterine artery and the elastography data in their study.[14] Ertikin investigated the umbilical artery RI and PI values in addition to uterine arteries in the study, and investigated whether there was a positive predictive contribution to placental insufficiency. As a result, they found an inverse correlation between strain ratio values and umbilical artery RI values which is consistent with the present study findings.[22] Pulsatility index of the uterine arteries is a useful screening parameter for the risk of pregnancy-induced hypertension. In general, uterine artery pulsatility index starts reducing with advancing gestational age. It is never >1.54 after 21 weeks of gestation. The diastolic flow is continuous without any notching in the uterine artery wave form.[23] The upper limit of the reference range is 1.17 after 28 weeks of gestation. In the present study, the uterine artery PI shown was in the range of 0.77 to 1.41 and uterine artery RI was in the range 0.38 to 0.77. Gomez *et al.*, have observed that progressively increasing pulsatility index of uterine arteries is associated with hypermature placenta and low fetal birth weight.[24] Karaman E *et al.*, studied the stiffness of placenta on sonoelastography in 107 patients. They measured the placental stiffness at three places – fetal edge, maternal edge and central portion of the placenta. They observed that the placental stiffness was significantly higher in pre-eclampsia patients as compared to normal controls.[18] This increase in placental stiffness in pregnancy- induced hypertension patients is also in accordance with the study of Kilic F *et al.* [15] Similar findings were also observed in the study of Habibi A *et al.* [25] Fujita *et al.* evaluated placental elasticity in pregnant women between 16 and 32 weeks and observed development of PE. Shear wave velocity values, which directly correlate with tissue stiffness, were significantly higher in the PE onset group compared to the non-onset group.[26] This is consistent with the present study results where the median SWE was 2.92 kPa which was higher among patients with elevated BP compared to normal patients with SWE median of 1.7 kPa which showed statistically significant. The median SWV was also higher among patients with elevated BP with median SWV of 1.41 m/s compared to normal patients with median of 0.90 m/s with statistical significance. The study reported a cut-off value of 1.188 m/s for predicting PE with sensitivity, specificity, PPV and NPV of 92.3%, 91.3%, 40.0% and 99.5% respectively.[26] In our study, the cut off value of placental SWE and placental SWV to predict the pregnancy induced hypertension for placental SWE was 1.27 kPa and placental shear wave velocity 1.15m/s. In Meena *et al.*, study the cut-off value of shear modulus was 2.96 kPa with sensitivity, specificity, PPV and NPV of 92%, 91.75%, 57.5% and 98.9%, respectively, and area under ROC 0.97.[27] In the present study the SWE was higher than normal in a few patients suggesting there is a risk of developing preeclampsia, similarly the median SWV was higher than normal in a few patients suggesting a possible risk of preeclampsia. According to a study by Herman and Harris, any transient temperature rise due to pulse bursts of ARFI may still be within the safe limit determined by the US Food and Drug Administration.[11] Sugitani *et al.* investigated the biological effects of ARFI on placental tissue and did not observe any histological evidence of thermal damage.[12] Although no harmful effects have been reported, judicious use of ARFI is recommended along with the least possible time of examination. Considering this safety issue, in the present study only one observer was involved in evaluation of elastography negating the possible harmful effects.

CONCLUSION

Placental elastography will act as an adjunct to clinical evaluation and ultrasonography in pregnancy-induced hypertension. Stiffer placentae will result in intra-uterine growth restriction, low birth weight babies and poor pregnancy outcome. In the present study, placental elasticity is found to be inversely proportional to the umbilical and uterine artery doppler parameters. Hence, placental elasticity can be used for assessing placental abnormalities in addition to other methods, but further studies are needed to use placental elasticity as a positive or negative predictive marker for placental insufficiency.

LIMITATIONS: Our study was a Cross sectional study, therefore, follow up of patients could not be performed.
CONFLICT OF INTEREST: None.

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